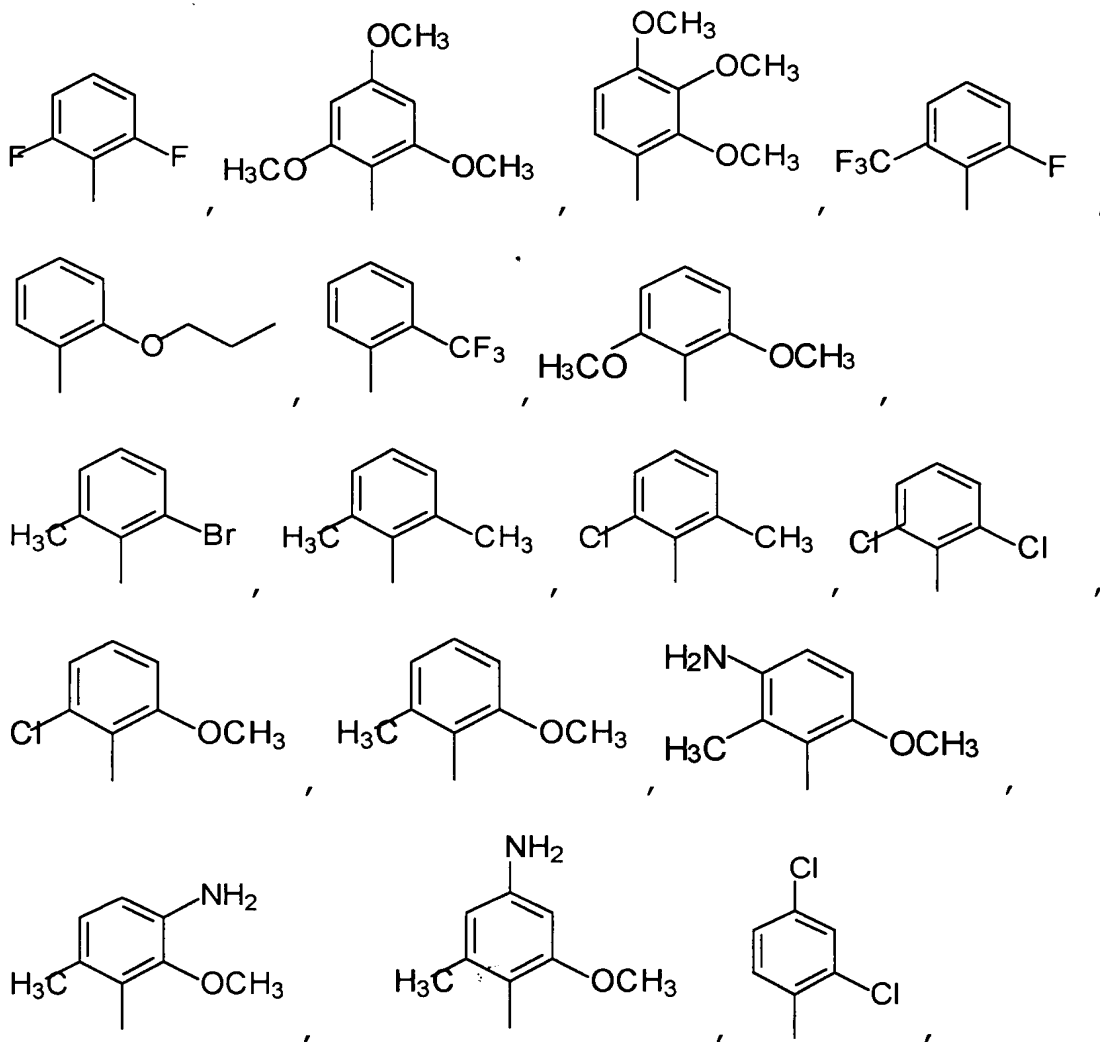
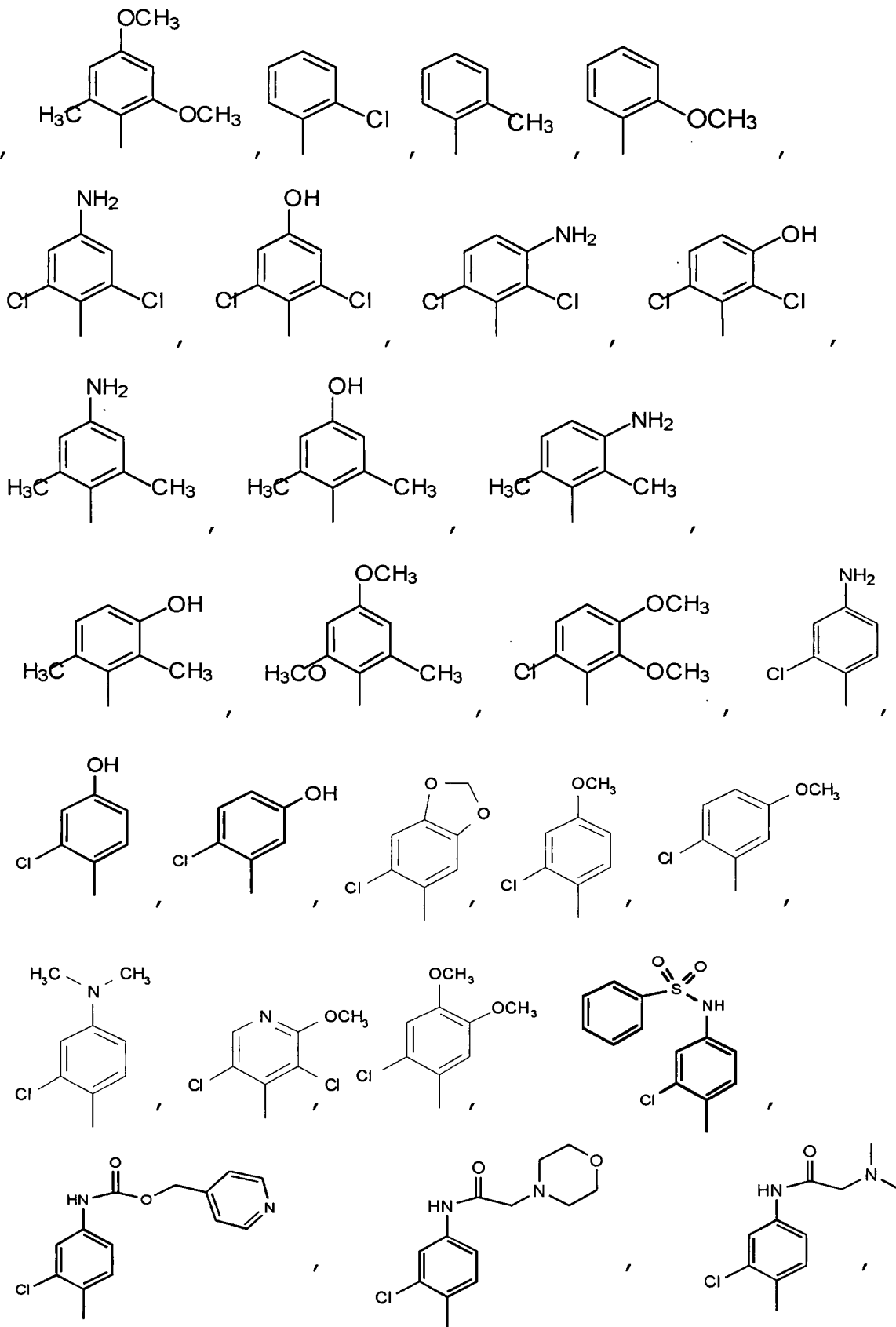


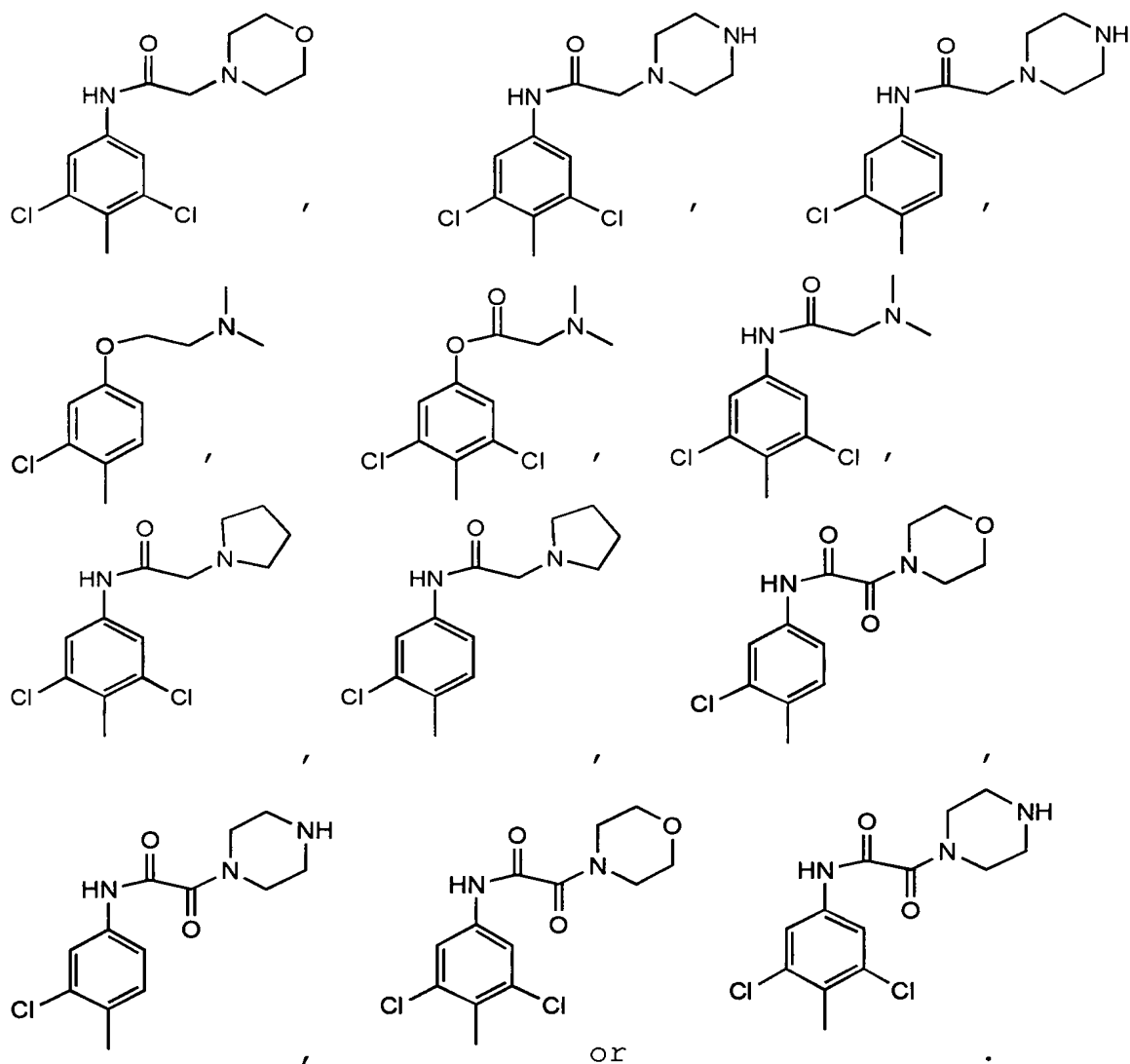
wherein Q_1 is selected from:



B²



B



B³ 9. (Twice amended) The compound according to claim 38, wherein X is selected from -S-, -O-, -S(O₂)-, -S(O)-, -NR²-, -C(R²)₂- or -C(O)-.

B⁴ 18. (Twice amended) The compound according to claim 38, wherein Q₃ substituted with 2 to 4 substituents,

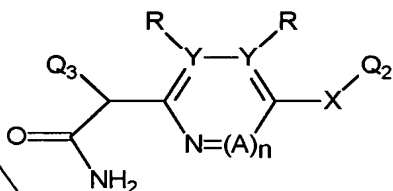
122

B

wherein at least one of said substituents is present in the ortho position relative to the point of attachment of Q₃ to the compound.

21. (Amended) The compound according to claim 19, wherein Q₃ contains 1 to 2 substituents in addition to said ortho substituents, said additional substituents being independently selected from NR'₂, OR', CO₂R', CN, N(R')C(O)R⁴; N(R')C(O)OR⁴; N(R')C(O)C(O)R⁴; N(R')S(O₂)R⁴; N(R')R⁴; N(R⁴)₂; OR⁴; OC(O)R⁴; OP(O)₃H₂; or N=CH-N(R')₂.

22. (Twice amended) The compound according to claim 38, wherein said compound is a compound of formula Ie:



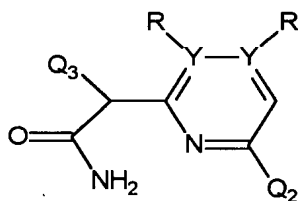
and is selected from any one of the following compounds:

cpd #	structure	cpd #	structure
201		206	

Sub C3 cont

cpd #	structure	cpd #	structure
203		207	
204		208	
205		209	

23. (Twice amended) The compound according to claim 38, wherein said compound is a compound of formula Ig:



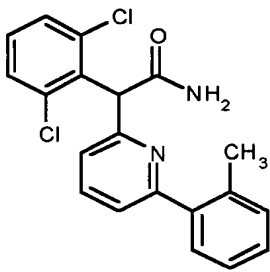
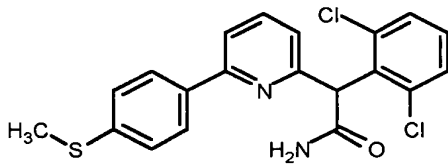
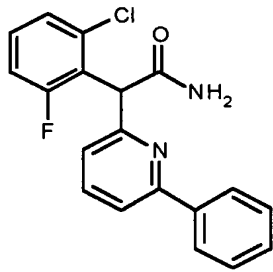
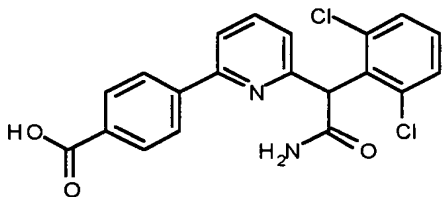
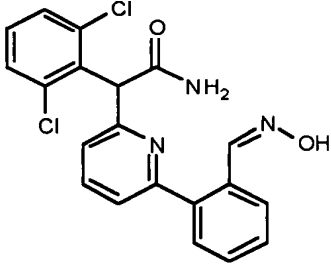
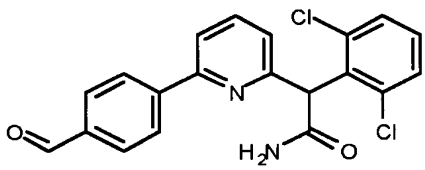
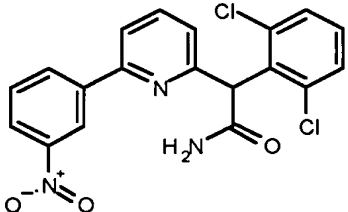
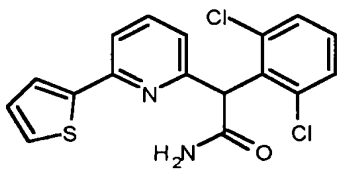
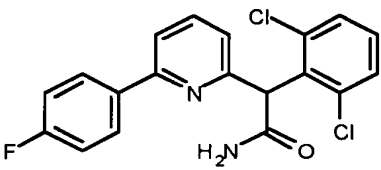
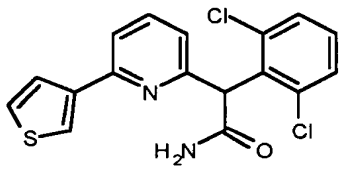
and is selected from any one of the following compounds:

B

cpd #	structure	cpd #	structure
202/ 301		310	
302		311	
303		312	
304		313	

Sub
C3
Cont

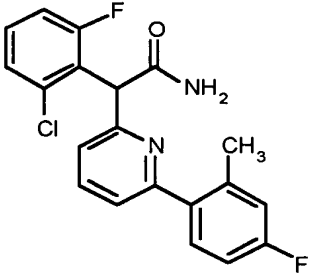
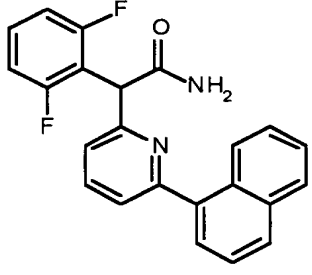
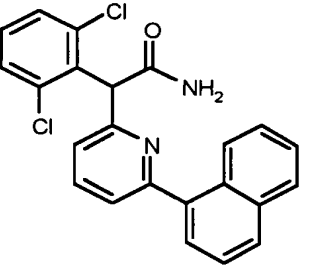
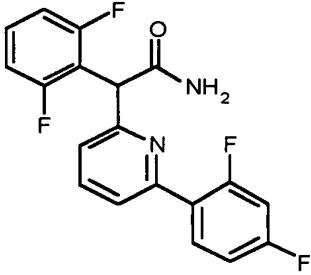
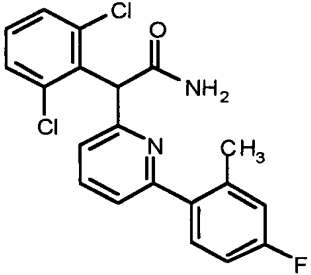
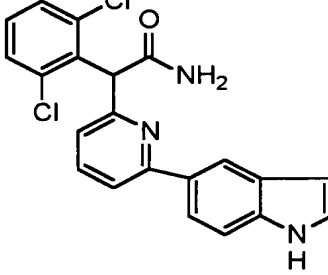
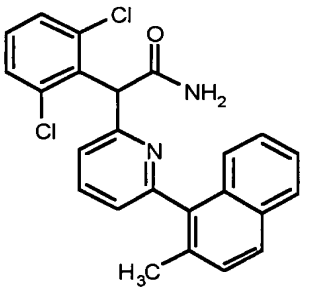
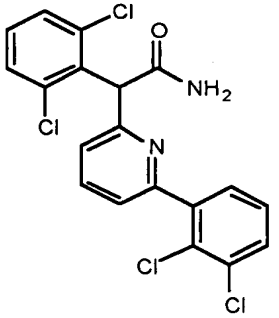
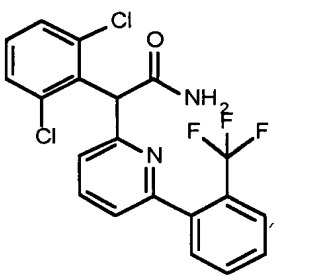
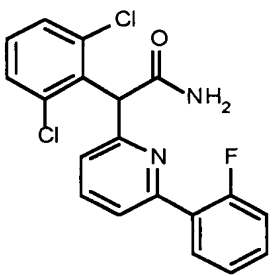
B

305		314	
306		315	
307		316	
308		317	
309		318	

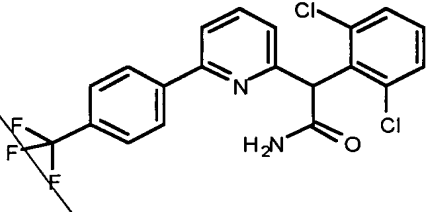
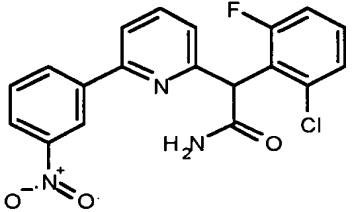
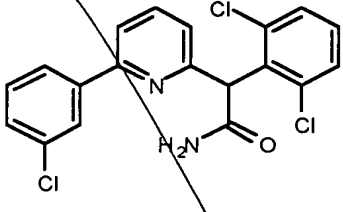
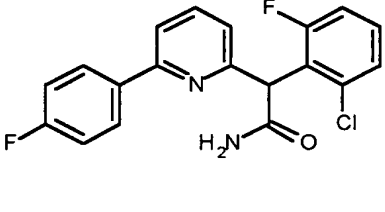
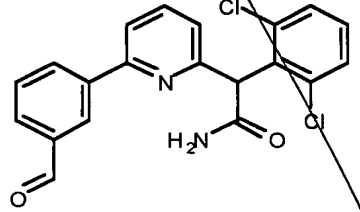
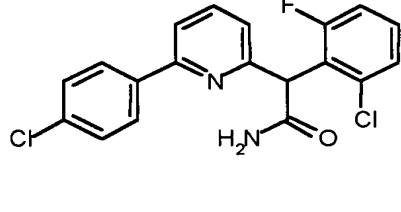
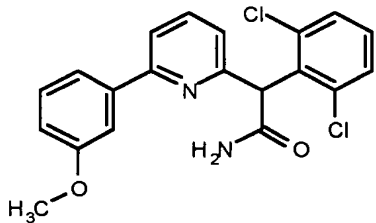
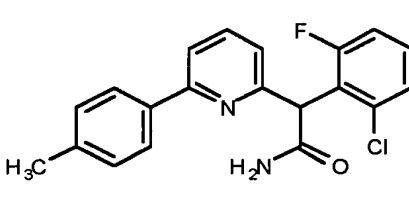
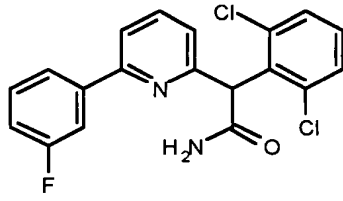
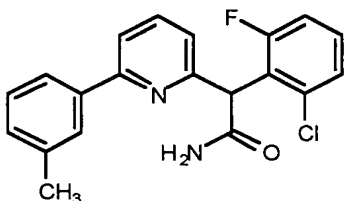
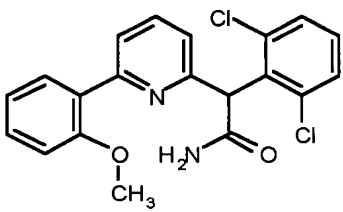
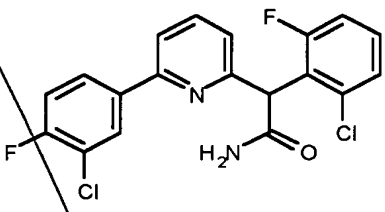
Sub
C3
Cont

B

85
sub
C3
cont

361		370	
362		371	
363		372	
373		382	
374		383	

B

319		328	
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323		332	
324		333	

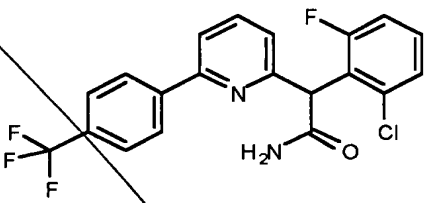
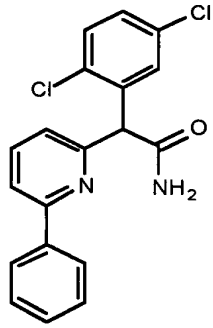
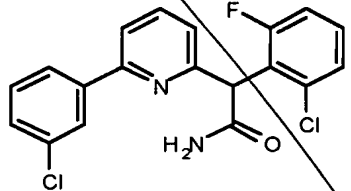
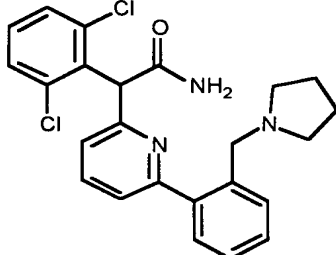
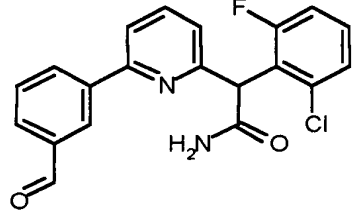
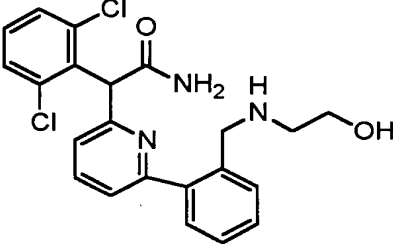
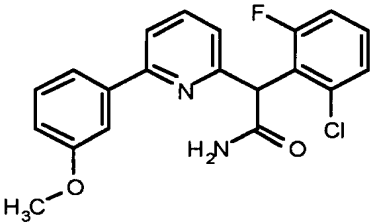
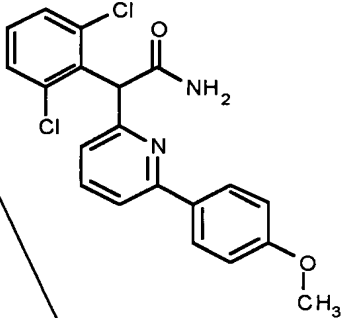
Sub
C3

B

325		334	
326		335	
327		336	
337		346	
338		347	
339		348	

Sub
C3

B

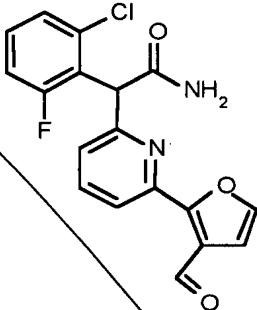
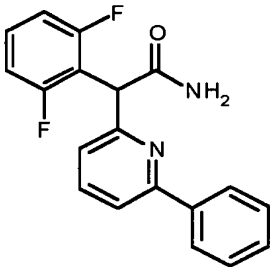
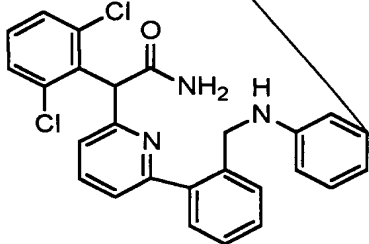
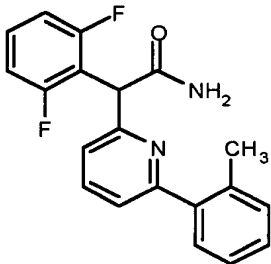
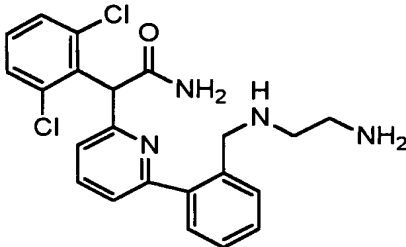
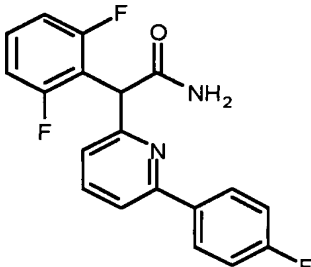
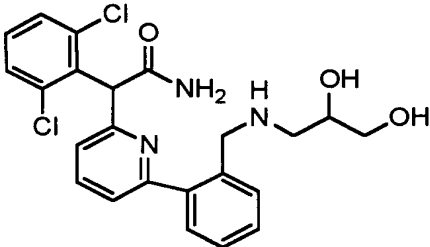
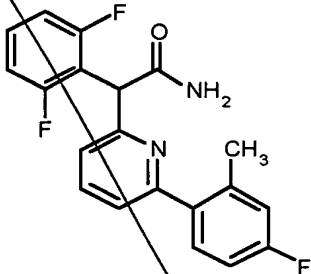
<p>340</p>		<p>349</p>	
<p>341</p>		<p>350</p>	
<p>342</p>		<p>351</p>	
<p>343</p>		<p>352</p>	

B

~~Sub~~
C3

344		353	
345		354	
355		364	
356		365	

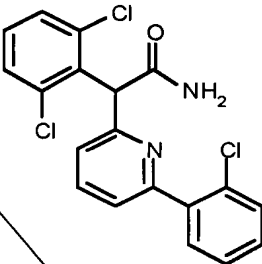
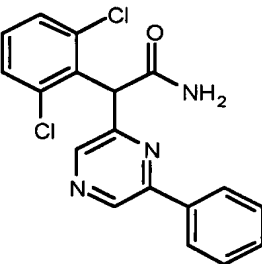
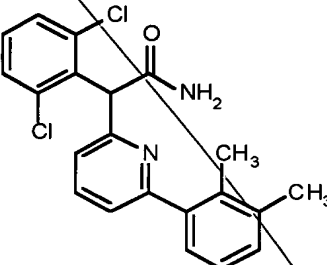
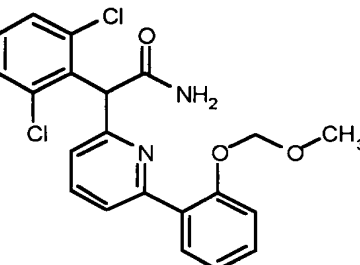
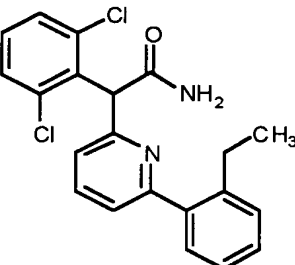
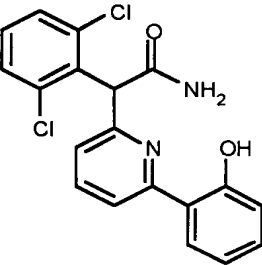
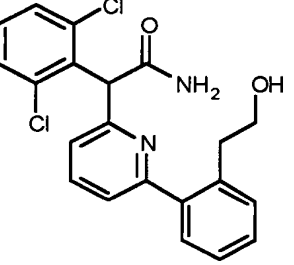
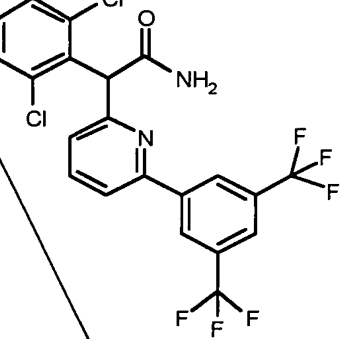
B

357		366	
358		367	
359		368	
360		369	

BS
sub
C3
cont

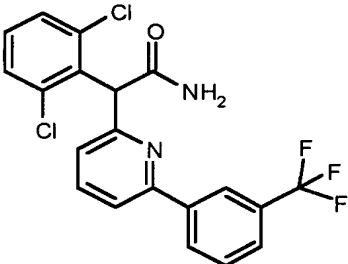
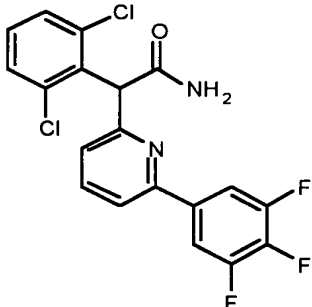
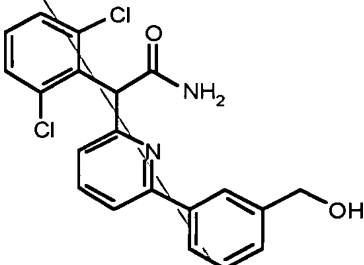
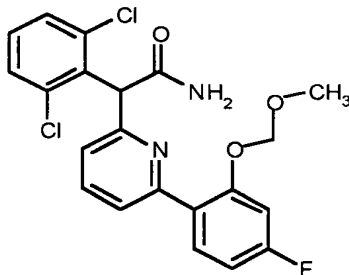
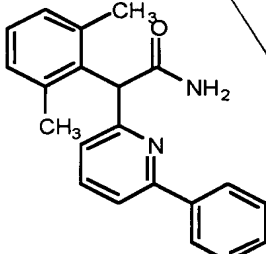
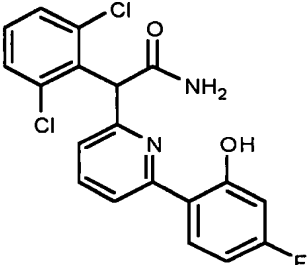
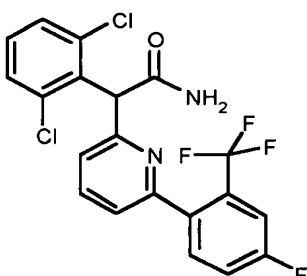
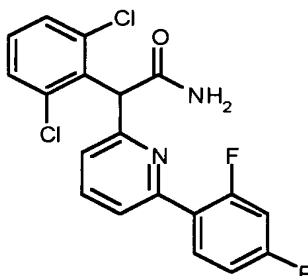
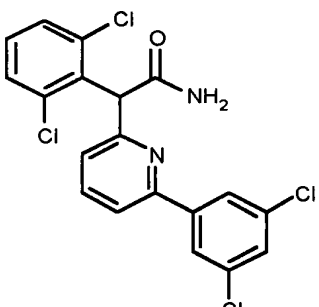
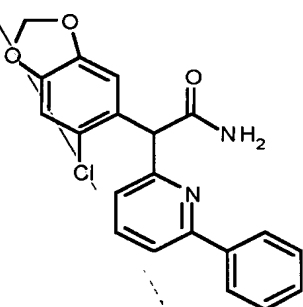
B

Sub
C3
cont

375		384	
376		385	
377		386	
378		387	

B

Sub
C3
cont

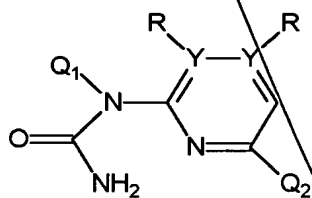
379		388	
380		389	
381		390	
391		396	
392		397	

B

~~88~~
sub
C3
cont

393		398	
394		399	
395		1301	

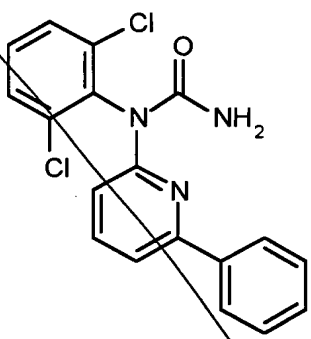
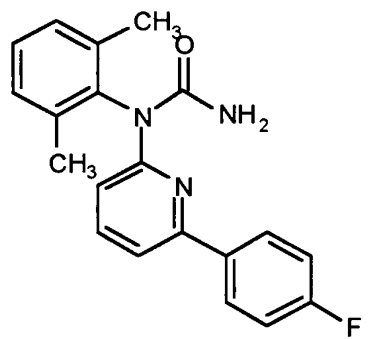
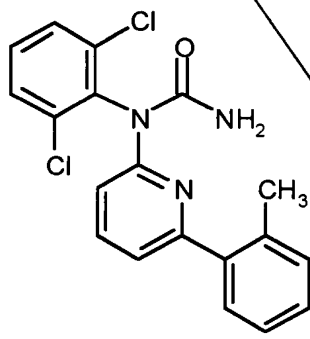
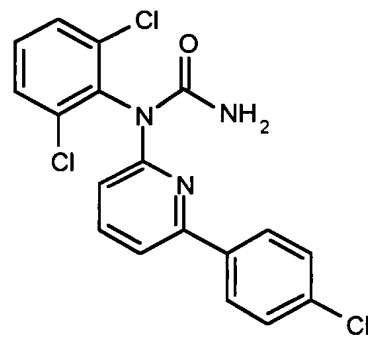
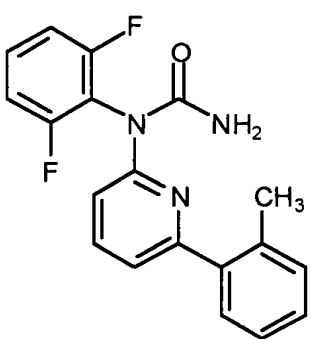
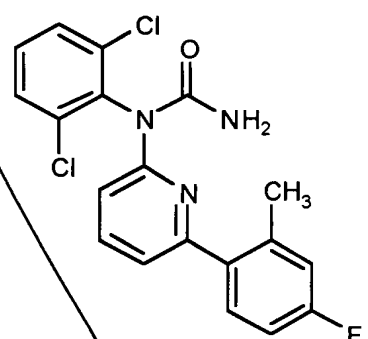
24. (Twice amended) The compound according to claim 38, wherein said compound is a compound of formula Ih:



and is selected from any one of the following compounds:

B

Sub
C3
cont

cpd #	structure	Cpd #	structure
401		407	
402		408	
403		409	

B

Sub
C3
cont

cpd #	structure	Cpd #	structure
404		410	
405		411	
406		412	

26. A method of treating inflammatory diseases, autoimmune diseases, viral diseases, destructive bone disorders, proliferative disorders, infectious diseases, neurodegenerative diseases, reperfusion/ischemia in stroke, myocardial ischemia, renal ischemia, heart attacks, angiogenic disorders, organ hypoxia, vascular hyperplasia, cardiac hypertrophy, thrombin-induced platelet aggregation or

B6

Sub
F1

B

B⁶ [conditions associated with prostaglandin endoperoxide synthase-2 in a patient, said method comprising administering to said patient a composition according to claim 25.

21
27. (Amended) The method according to claim ²⁰26, wherein said method is used to treat an inflammatory disease selected from acute pancreatitis, chronic pancreatitis, asthma, allergies, or adult respiratory distress syndrome.

Sub F2
28. (Amended) The method according to claim 26, wherein said method is used to treat an autoimmune disease selected from glomerulonephritis, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Graves' disease, autoimmune gastritis, diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, psoriasis, or graft vs. host disease.

Sub C4
29. (Amended) The method according to claim 26, wherein said method is used to treat a destructive bone disorders selected from osteoarthritis, osteoporosis or multiple myeloma-related bone disorder.

30. (Amended) The method according to claim 26, wherein said method is used to treat a proliferative disease selected from acute myelogenous leukemia, chronic myelogenous leukemia, metastatic melanoma, Kaposi's sarcoma, or multiple myeloma.

L 31. (Amended) The method according to claim 26,

B⁶ wherein said method is used to treat an infectious disease selected from sepsis, septic shock, or Shigellosis.

32. (Amended) The method according to claim 26, wherein said method is used to treat a viral disease selected from acute hepatitis infection, HIV infection or CMV retinitis.

33. (Amended) The method according to claim 26, wherein said method is used to treat a neurodegenerative disease selected from Alzheimer's disease, Parkinson's disease, cerebral ischemia or neurodegenerative disease caused by traumatic injury.

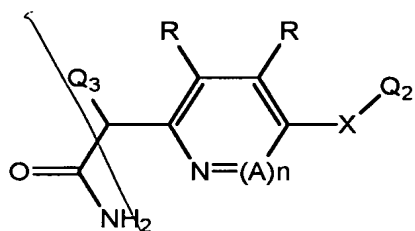
Sub F₃ 34. (Amended) The method according to claim 26, wherein said method is used to treat ischemia/reperfusion in stroke or myocardial ischemia, renal ischemia, heart attacks, organ hypoxia or thrombin-induced platelet aggregation.

35. (Amended) The method according to claim 26, wherein said method is used to treat a condition associated with prostaglandin endoperoxide synthase-2 selected from edema, fever, analgesia or pain.

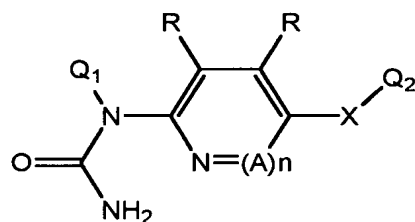
B⁷ 37. (Amended) The method according to claim 26, wherein said method is used to treat an angiogenic disorder selected from solid tumors, ocular neovascularization, or infantile haemangiomas.

Sub C⁵ 38. (Amended) A compound of the formula:

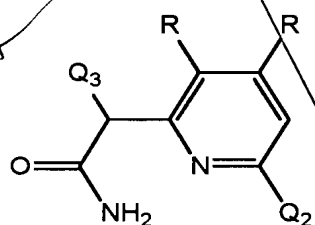
B



(Ie)

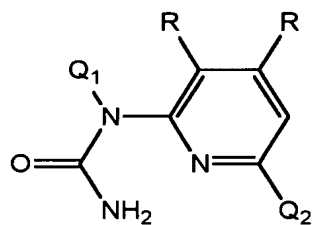


(If)



(Ig)

, or



(Ih)

wherein:

Q_3 is a 5-6 membered aromatic carbocyclic or heterocyclic ring system; or an 8-10 membered bicyclic ring system comprising aromatic carbocyclic rings, aromatic heterocyclic rings or a combination of an aromatic carbocyclic ring and an aromatic heterocyclic ring; wherein Q_3 is substituted with 1 to 4 substituents, each of which is independently selected from halo; C_1 - C_3 alkyl optionally substituted with NR'_2 , OR' , CO_2R' or $CONR'_2$; O -(C_1 - C_3)-alkyl optionally substituted with NR'_2 , OR' , CO_2R' or $CONR'_2$; NR'_2 ; OCF_3 ; CF_3 ; NO_2 ; CO_2R' ; $CONHR'$; SR' ; $S(O_2)N(R')_2$; SCF_3 ; CN ; $N(R')C(O)R^4$; $N(R')C(O)OR^4$; $N(R')C(O)C(O)R^4$; $N(R')S(O_2)R^4$; $N(R')R^4$; $N(R^4)_2$; OR^4 ; $OC(O)R^4$; $OP(O)_3H_2$; or $N=CH-N(R')_2$;

B

each of Q₁ and Q₂ are independently selected from 5-6 membered aromatic carbocyclic or heterocyclic ring systems, or 8-10 membered bicyclic ring systems consisting of aromatic carbocyclic rings, aromatic heterocyclic rings or a combination of an aromatic carbocyclic ring and an aromatic heterocyclic ring; wherein:

Q₁ is substituted with 1 to 4 substituents, independently selected from halo; C₁-C₃ alkyl optionally substituted with NR'₂, OR', CO₂R' or CONR'₂; O-(C₁-C₃)-alkyl optionally substituted with NR'₂, OR', CO₂R' or CONR'₂; NR'₂; OCF₃; CF₃; NO₂; CO₂R'; CONHR'; SR'; S(O₂)N(R')₂; SCF₃; CN; N(R')C(O)R⁴; N(R')C(O)OR⁴; N(R')C(O)C(O)R⁴; N(R')S(O₂)R⁴; N(R')R⁴; N(R⁴)₂; OR⁴; OC(O)R⁴; OP(O)₃H₂; or N=CH-N(R')₂; and

Q₂ is optionally substituted with up to 4 substituents, independently selected from halo, CH=N-OH, or CH=O; C₁-C₃ straight or branched alkyl optionally substituted with NR'₂, OR', CO₂R', S(O₂)N(R')₂, N=CH-N(R')₂, R³, NH-CH₃, NHCH₂CH₂OH, NHCH₂CH(OH)CH₂OH, CH₂OCH₂OCH₃, NHCH₂CH₂NH₂, NH-phenyl, piperazinyl, pyrrolidinyl or CONR'₂; O-(C₁-C₃)-alkyl optionally substituted with NR'₂, OR', CO₂R', S(O₂)N(R')₂, N=CH-N(R')₂, R³, or CONR'₂; NR'₂; OCF₃; CF₃; NO₂; CO₂R'; CONHR'; R³; OR³; NHR³; SR³; C(O)R³; C(O)N(R')R³; C(O)OR³; SR'; S(O₂)N(R')₂; SCF₃; N=CH-N(R')₂; CH=N-OH; CH=O; or CN;

B

wherein R' is selected from hydrogen, (C₁-C₃)-alkyl; (C₂-C₃)-alkenyl or alkynyl; phenyl or phenyl substituted with 1 to 3 substituents independently selected from halo, methoxy, cyano, nitro, amino, hydroxy, methyl or ethyl;

R³ is selected from a 5-6 membered aromatic carbocyclic or heterocyclic ring system; and

R⁴ is (C₁-C₄)-alkyl optionally substituted with N(R')₂, OR', CO₂R', CON(R')₂, or SO₂N(R²)₂; or a 5-6 membered carbocyclic or heterocyclic ring system optionally substituted with N(R')₂, OR', CO₂R', CON(R')₂, or SO₂N(R²)₂;

X is selected from -S-, -O-, -S(O₂)-, -S(O)-, -S(O₂)-, N(R²)-, -N(R²)-S(O₂)-, -N(R²)-C(O)O-, -O-C(O)-N(R²), -C(O)-, -C(O)O-, -O-C(O)-, -C(O)-N(R²)-, -N(R²)-C(O)-, -N(R²)-, -C(R²)₂-, -C(OR²)₂-, -CH(OH)-;

each R is independently selected from hydrogen, -R², -N(R²)₂, -OR², SR², -C(O)-N(R²)₂, -S(O₂)-N(R²)₂, or -C(O)-OR², wherein two adjacent R are optionally bound to one another and, together with each Y to which they are respectively bound, form a 4-8 membered carbocyclic or heterocyclic ring;

R² is selected from hydrogen, (C₁-C₃)-alkyl, or (C₁-C₃)-alkenyl; each optionally substituted with -N(R')₂, -OR', SR', -C(O)-N(R')₂, -S(O₂)-N(R')₂, -C(O)-OR', or R³;

Y is C;

A is CR'; and

BT
sub
C's
n is 1; wherein an aromatic heterocyclic ring system
comprises 1-2 heteroatoms independently selected from N, O or
S.

B



2

APPLICANT GUY W. BEMIS ET AL

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TITLE: LABORATORS OF p38

66/81/90



PAGES OF APPLICATION 125

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NUMBER OF CLAIMS 37 SHEETS OF DRAWING 10

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CHECK IN THE AMOUNT OF \$936.00

ASSIGNMENT RECORDATION FORM COVER SHEET

ASSIGNMENT & CHECK IN THE AMOUNT OF \$40.00

VERIFIED STATEMENT OF SMALL ENTITY STATUS

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